

LEARNING OBJECTIVES

- 1.08.01 Identify the function of the following cell structures:
- a. Cell membrane
 - b. Cytoplasm
 - c. Mitochondria
 - d. Lysosome
 - e. Nucleus
 - f. DNA
 - g. Chromosomes
- 1.08.02 Identify effects of radiation on cell structures.
- 1.08.03 Identify the law of Bergonie and Tribondeau.
- 1.08.04 Identify factors which affect the radiosensitivity of cells.
- 1.08.05 Given a list of types of cells, identify which are most or least radiosensitive.
- 1.08.06 Identify primary and secondary reactions on cells produced by ionizing radiation.
- 1.08.07 Identify the following definitions and give examples of each:
- a. Stochastic effect
 - b. Non-stochastic effect
- 1.08.08 Identify the LD 50/30 value for humans.
- 1.08.09 Identify the possible somatic effects of chronic exposure to radiation.
- 1.08.10 Distinguish between the three types of the acute radiation syndrome, and identify the exposure levels and the symptoms associated with each.
- 1.08.11 Identify risks of radiation exposure to the developing embryo and fetus.
- 1.08.12 Distinguish between the terms "somatic" and "heritable" (or "genetic") as they apply to biological effects.

INTRODUCTION

Within a year after Roentgen's discovery of X-rays in 1895, it was learned that exposure to ionizing radiation could lead to biological damage. Since that time, a tremendous amount of research has been done attempting to interpret the reactions which take place from the moment that radiation enters a living cell until some permanent damage is produced. From beginning to end, these initial reactions are probably completed in a millionth of a second, making them very difficult to study. For this reason, it is still not known which of the many chemical or biochemical reactions brought about by ionizing radiation are responsible for initiating biological damage.

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- a. Cell membrane*
- b. Cytoplasm*
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- e. Nucleus*
- f. DNA*
- g. Chromosomes*

CELL STRUCTURE

Since the primary site of radiation damage is in the cell, the logical place to start a study of the biological effects of radiation is with the structure of this basic unit of all living material.

Cells are the building blocks of which man and his living environment are composed; they are the fundamental unit of which all living organisms are made. Although there is no such thing as a typical cell, all cells have several features in common.

Most cells are composed of protoplasm: a mixture of carbohydrates, lipids, proteins, nucleic acids, inorganic salts, gases and between 70 and 80% water. The cell may be subdivided into three major parts: (1) the cell membrane; (2) the cytoplasm; and (3) the nucleus. (*See Figure 1*)

BASIC CELL STRUCTURE

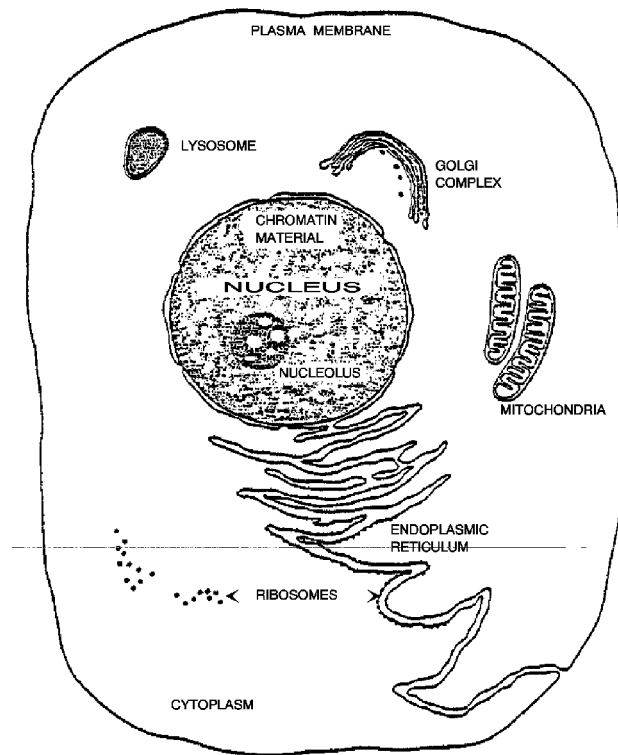


Figure 1

Cell Membrane. The cell membrane is only 100 angstrom units (a millionth of a centimeter) thick, and is a living functional part of the cell. It helps to regulate the concentration of water, salts, and organic matter which form the interior environment of the cell. In red blood cells, and nerve cells, the membrane distinguishes between sodium and potassium ions even though these ions are alike in size and electrical charge. The membrane actively transports potassium ions into the cell and opposes the entrance of sodium ions. The membrane is thus capable of "active transport." In addition, all food entering the cell and all waste products or secretions leaving it must pass through this membrane.

Cytoplasm. The cytoplasm is a jelly like substance in which the nucleus is suspended; it is encased within the cell membrane. This material is an aqueous solution of soluble proteins and salts which constitutes the interior environment of the cell.

Many small functional units called organelles are contained in the cytoplasm. Principle among these are the mitochondria, which are the "power plants" of both plant and animal cells. It is here that oxygen is used for the oxidation of essential foodstuffs and the formation of carbon dioxide. The metabolic energy so released is captured in the chemical bonds of a special energy storing molecule known as ATP (adenosine triphosphate). This molecule supplies the energy for all the activities of the cell, including reproduction.

The lysosomes contain the digestive enzymes that break down large molecules, such as those of fats, proteins, and nucleic acids, into smaller constituents that can be oxidized by the oxidative enzymes of the mitochondria. The lysosomal membrane isolates the digestive enzymes from the rest of the cytoplasm. Rupture of the membrane and release of the enzymes leads to the dissolution of the cell.

Nucleus. Each cell contains a small, usually oval, body known as the nucleus. In some cells this has a relatively fixed position and is found near the center; in others it may move around freely and be found almost anywhere in the cell. The nucleus is an important center of control of the cell, directing cellular activity and containing the hereditary factors (genes) responsible for the traits of the animal or plant.

The membrane surrounding the nucleus and separating it from the adjacent cytoplasm is called the nuclear membrane. It is a double membrane with annuli, or holes, in the outer layer, open to the cytoplasm. This suggests that the cytoplasm of the cell is in direct communication with the protoplasm of the cell nucleus (the nucleoplasm). The function of this nuclear membrane is to regulate the constant flow of materials into and out of the nucleus.

The nucleoli are spherical bodies which are found within the cell nucleus. These cell constituents are packed with tiny granules similar to the ribosomes of the cytoplasm. The nucleoli are rich in RNA and appear to be active centers of protein and RNA synthesis.

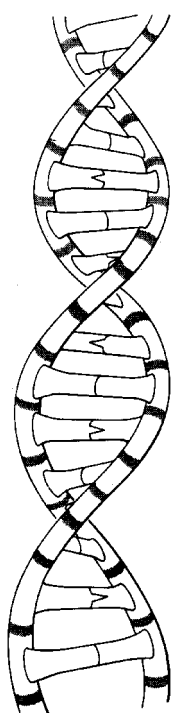


Figure 2.
Double Helix

DNA (DeoxyriboNucleic Acid) is the most important material making up the chromosomes and serves as the master blueprint for the cell. It determines what types of RNA are produced which, in turn, determine the types of protein that are produced. It is generally assumed to take the form of a twisted ladder or double helix. (See Figure 2)

The sides of the ladder are strands of alternating sugar and phosphate groups. Branching off from each sugar group is one of four nitrogenous bases: cytosine, thymine, adenine and guanine. (See Figure 3) The rungs of the ladder consist of two nitrogenous bases, one from each strand, linked by hydrogen bonds. Cytosine is always paired with guanine and thymine is always paired with adenine. A section of DNA that codes for one protein is referred to a gene although the 'message' from several genes can be carried by single piece of RNA.

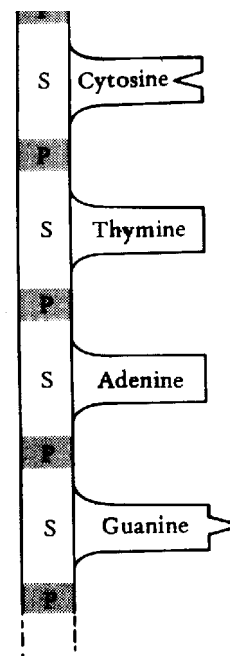


Figure 3.
DNA Base Pairs

Chromosomes consist of highly convoluted supercoils of DNA and associated protein. Each chromosome possesses a single centromere, a short specialized section of the chromosome that serves as a type of attachment point. The centromere must be present for the appropriate movement of the chromosomes during cell division. To ensure its survival, each new cell must possess all the required DNA (a complete chromosome complement).

1.08.02 *Identify effects of radiation on cell structures.***RADIATION EFFECTS ON CELL CONSTITUENTS**

A great deal of work has been performed on examining the effects of radiation on various organelles. The following dose rates apply to human cells.

It has been established it takes about 3,000 to 5,000 rads of absorbed dose to rupture the **cell membrane**. This major injury to the cell allows the extracellular fluids to enter into the cell. Inversely, it also allows leakage out of ions and nutrients which the cell brought inside. Membrane rupture may result in the death of a cell, in this case death would be compared to drowning. Large doses below 3,000 rads increase the permeability of the cell membrane and some leakage occurs.

Radiation effects on cytoplasm are negligible compared to observed effects on structures which are suspended within it. The first involve the **mitochondria**. It requires a few thousand rad to disrupt their function. This results in the immediate interruption of the cell's food supply (ATP). If the cell has a large reserve of ATP it can repair the damage to the mitochondria and then continue to produce ATP. The greater the dose received, the longer the repair time will be. If the stored food supply is not adequate to nourish the cell during repair, then the cell will die from starvation.

Another organelle within the cytoplasm that is effected by radiation is the lysosome. The **lysosome** will be ruptured at dose levels between 500 and 1,000 rads. When this occurs, the enzymes are released within the cell and begin digesting structures of the cell. This cell death can be compared with suicide. At much larger doses the digestive enzymes are rendered inactive.

The most radiologically sensitive part of the cell is the **nucleus**. Because there is a wide band of sensitivity for cell nuclei, quantifying a dose range is difficult. The major effect of radiation on the cell nucleus is the inhibition of **DNA** replication. This means that the cell is unable to prepare for division. Before a cell divides it produces a complete duplicate set of **chromosomes** which carry all the information needed to reproduce the organism. With damaged DNA, duplicate chromosomes cannot be manufactured. If this process is delayed long enough, the cell dies and the death of the cell can be compared to death in childbirth. At lower doses DNA production is delayed only a short time. As the dose is increased, the delay period gets longer until death occurs.

1.08.03 *Identify the law of Bergonie and Tribondeau.*

RADIOSENSITIVITY AND THE LAW OF BERGONIE AND TRIBONDEAU

As early as 1906 an attempt was made to correlate the differences in sensitivity of various cells with differences in cellular physiology. These differences in sensitivity are stated in the Law of Bergonie and Tribondeau: "*The radiosensitivity of a tissue is directly proportional to its reproductive capacity and inversely proportional to its degree of differentiation.*" In other words, cells most active in reproducing themselves and cells not fully mature will be most harmed by radiation. This law is considered to be a rule-of-thumb, with some cells and tissues showing exceptions.

1.08.04 *Identify factors which affect the radiosensitivity of cells.*

Since the time that the Law of Bergonie and Tribondeau was formulated, it is generally accepted that cells tend to be radiosensitive if they are:

1. Cells that have a *high division rate*.
2. Cells that have a *high metabolic rate*.
3. Cells that are of a *non-specialized type*.
4. Cells that are well *nourished*.

1.08.05 Given a list of types of cells, identify which are most or least radiosensitive.

The law can be used to classify the following tissues as **radiosensitive**:

1. Germinal (reproductive) cells of the ovary and testis i.e., spermatogonia
2. Hematopoietic (bloodforming) tissues: red bone marrow, spleen, lymph nodes, thymus
3. Epithelium of the skin
4. Epithelium of the gastrointestinal tract (interstitial crypt cells)

The law can be used to classify the following tissues as **radioresistant**:

1. Bone
2. Liver
3. Kidney
4. Cartilage
5. Muscle
6. Nervous tissue.

1.08.06 Identify primary and secondary reactions on cells produced by ionizing radiation.

PRIMARY AND SECONDARY EFFECTS

A great many agents can cause injuries to the human cell. When such injury occurs, the effects are the same regardless of the agent which caused the damage. Ionizing radiation produces damage to cells, but in a mostly nonspecific way; that is, other physical and chemical substances cause the same effects because the body responds the same to certain cell damage regardless of the cause.

Radiation passing through living cells will directly ionize or excite atoms and molecules in the cell structure. These changes affect the forces which bind the atoms together into molecules. If the molecule breaks up (dissociates), the fragments are called free radicals and ions, and are not chemically stable. Free radicals are electrically neutral structures

with one unpaired electron. Because the cell has a higher water content, the most important free radicals are those formed from water molecules. For example, an excited H_2O^* molecule may dissociate into



in which the hydrogen radical H° has an unpaired e^- and the OH° radical will have nine e^- , one of which will be unpaired. The free radicals are very reactive chemically, and when combining can produce hydrogen peroxide (H_2O_2), which is a chemical poison and is the most harmful free radical product. Further effects are produced when the radicals and ions interact with other cell material. In this way, damage is caused in a direct and indirect manner. The role that each type of action plays in the total damage to the cell is still an unsolved problem. Of the damage which is done, the effects are greatest in the nucleus of the cell, but injury to the cytoplasm can also cause serious effects in the cell.

The total effect on cell processes is a function of the dose of radiation. The cell processes will be affected in varying degrees up to the ultimate result - cell death. Some damage to the cell may be repaired. This can be accomplished by action of the cell itself, or by replacement of badly injured cells in a given tissue through mitosis of healthy cells. On the other hand, if the extent of the damage to an organ is quite large, the organ may not be able to repair itself. That is, damaged cells may show confused growth but eventually be unable to divide. Or the cells may begin to exhibit uncontrolled growth. Although many factors are important in assessing the total damage, it seems likely that most cell functions and structures can be impaired by radiation.

1.08.07 *Identify the following definitions and give examples of each:*

- a. *Stochastic effect*
- b. *Non-stochastic effect*

STOCHASTIC EFFECTS

Stochastic effects are those in which the probability within a population of the effect occurring increases with dose, without threshold. Any dose, therefore, has a certain probability, however low, of causing the effect. Stochastic effects may result from injury to a single cell or a small number of cells. Carcinogenic (cancer) and genetic (capable of being inherited) effects are examples of stochastic effects. In these, once the effect is

induced, the severity is already determined by the nature of the effect.

Stochastic effects are assumed to have some chance of occurring no matter how low the dose. DOE dose limits intend to limit the probability of stochastic effects occurring to an acceptable level. That is, any exposure to radiation involves a risk, and no risk should be undertaken without the expectation of a net benefit.

NON-STOCHASTIC EFFECTS

Non-stochastic, or deterministic, effects are those in which the severity of the effect varies with the dose. For these types of effects, a threshold dose may exist. That is, if the dose is kept below the threshold dose, the effect will not be observed. Non-stochastic effects are considered to result from the collective injury of a substantial number of cells in the tissue. Examples of such effects are cataracts, skin ulcerations or burns, depletion of blood-forming cells in bone marrow, and impairment of fertility.

1.08.08 *Identify the LD 50/30 value for humans.*

LETHAL DOSE

Not only do various organisms vary in their sensitivity to radiation, but individuals of the same species also react differently. Because of this biological variability, the dose which is lethal to 50% of the individuals exposed is used. The concept used is LD 50/30. LD 50/30 is defined as the dose of radiation expected to cause death (Lethal Dose) within 30 days to 50% of those exposed, without medical treatment. The best estimate for the LD 50/30 for humans is between 300 and 500 rads, and is usually stated as 450 rad.

1.08.09 *Identify the possible somatic effects of chronic exposure to radiation.***EFFECTS OF CHRONIC EXPOSURES TO IONIZING RADIATION**

Chronic radiation exposure effects involve a low dose over a relatively long period of time (weeks to years). The effects, if any occur, do not manifest themselves until many years after the exposure. Other than radiation sickness associated with acute exposure, there is no unique disease from radiation, but only a statistical increase in existing conditions. The following section discusses possible chronic effects from exposure to ionizing radiation. One possible effect from acute and chronic exposure that has received much attention is genetically based. These effects are addressed in the next section.

Cancer. With proper selection of animal species, strains, and dose, ionizing radiation may be shown to exert an almost universal carcinogenic action resulting in tumors in a great variety of organs and tissues. There is human evidence as well that radiation may contribute to the induction of various kinds of neoplastic diseases. Human evidence of this includes radium dial painters; radiologists and dentists; uranium miners; and atomic bomb survivors. The main sites of solid tumors are the breast in women, thyroid, lung and some digestive organs. These tumors have long latent periods (approximately 10 to greater than 30 years) and occur in larger numbers than leukemia. Leukemia (abnormal increase in white blood cells) has a much shorter latent period. The incidence peaks within a few years of exposure and returns to normal levels after about 25 years.

Cataracts. The lens of the eye is highly susceptible to irreversible damage by radiation. When the cells of the lens become damaged, they lose their transparency and a cataract is thus formed. Exposures as small as 600 to 900 R may produce a cataract, although the symptoms and signs may not be apparent for years after the exposure. The damaging effects of penetrating radiation to the lens of the eye may be cumulative, and repeated small doses may result in cataract formation.

Radiation induced cataracts are produced primarily by neutron and gamma radiation. Experiments with animals and human case histories indicated that neutron radiation constitutes the greatest danger, with gamma radiation of slightly less importance.

Susceptibility to radiation induced cataract formation seems to be somewhat dependent on age. Radiation is more likely to produce cataracts in younger persons because of continuous growth of the lens (growing tissues are more radiosensitive).

Extensive irradiation of the eye may result in inflammation of the cornea or in an increase in tension within, and hardening of, the eyeball. These conditions usually become manifest several weeks after the exposure and may terminate in loss of vision.

Life Span. In a number of animal experiments, radiation has been demonstrated to shorten life span. The aging process is complex and largely obscure and the exact mechanisms involved in it are, as yet, uncertain. Irradiated animals in these investigations appear to die of the same diseases as non-irradiated controls, but they do so at an earlier age. How much of the total effect is due to premature aging and how much to an increased incidence of radiation induced diseases is still unresolved.

The study of small amounts of exposure to radiation for beneficial purposes is termed radiation hormesis. One pioneer in the field, Dr. Luckey of the University of Missouri, Columbia, stated in a 1982 article, "Extensive literature indicates that minute doses of ionizing radiation benefit animal growth and development, fecundity (ability to produce offspring), health and longevity. Specific improvements appear in neurological function, growth rate and survival of young, wound healing, immune competence, and resistance to infection, radiation morbidity (radiation sickness), and tumor induction and growth."

An extension of life and a lower incidence of cancer has been seen in rodents exposed to lower doses, (100 to 400 rads), over a lifetime.

1.08.10 Distinguish between the three types of the acute radiation syndrome, and identify the exposure levels and the symptoms associated with each.

ACUTE EFFECTS

Acute effects are classified as effects that occur within 1-2 months of the exposure. This definition is somewhat arbitrary in view of the various factors that can affect the length of time between the exposure and the effect. Normally, acute effects are only observed if the dose is greater than 10 rads and delivered over a short time (acutely).

At high dose rates the body repair mechanisms become less effective and the differences in the biological damage from low LET radiation disappear. As such, the concept of the dose equivalent does not apply to acute exposures greater than 15 rem. Above this, the exposure should only be expressed as a dose in rads. For example, the dose from gammas that would kill 50% of an exposed human population is estimated to be from 350 to 450

rads, one to two times the required neutron dose. At low doses however, the dose from gammas typically needs to be 5 to 10 times the neutron dose to produce comparable effects.

RADIATION SYNDROMES AND STAGES IN MAN

A syndrome is a combination of symptoms resulting from a single cause and occurring together so as to constitute a single clinical picture.

Large acute whole-body exposures in man may result in one of three radiation syndromes. At the lowest doses sufficient to produce one of these syndromes (200 - 1,000 rads) the primary affected tissue is the hematopoietic system. At higher doses (1,000 - 5,000 rads) the gastrointestinal tract is the critical tissue, although the hematopoietic system is also greatly affected. Above 5,000 rads we say that the dominant effects involve the central nervous system even though the hematopoietic system and gastrointestinal tract have been effectively destroyed by such a dose.

Each syndrome can be considered to progress through the following four stages: the prodromal (initial) stage; the latent phase; a period of illness; and recovery or death.

Prodromal Stage. This is the first set of symptoms that occurs following a sufficiently large acute dose. The symptoms may include nausea, vomiting and diarrhea (NVD) as well as anorexia (loss of appetite) and fatigue. The actual causes of the prodromal symptoms are unknown. To some degree, the time of onset of these symptoms is indicative of the magnitude of the dose, however, the appearance of these symptoms, especially nausea and vomiting, can also be induced psychologically.

Latent Phase. This is an asymptomatic period between the prodromal stage and the onset of symptoms of later stages. The higher the dose the shorter the latent phase. At sufficiently high doses the latent phase effectively disappears.

Illness. Many of the characteristics of the prodromal stage reoccur along with a variety of additional symptoms, i.e., ulcerations about the mouth, fever, etc.

Recovery or Death. With an acute dose above 1,000 rads, death is probably certain, even with the best of medical care. It is generally believed that without medical attention death is certain above 600 rads.

HEMATOPOIETIC SYNDROME

The hematopoietic system syndrome is produced by acute whole body doses of 200 to 1,000 rads. Death, if it occurs, will primarily be a result of damage to the hematopoietic (blood forming) organs: red bone marrow, lymph nodes, spleen and thymus. Damage to other systems, notably the gastrointestinal tract, will also play a role.

Effects of Radiation on Blood Cells.

Lymphocytes. These are a type of leukocyte (white blood cell) responsible for antibody production. Lymphocytes are formed in the lymph nodes, the thymus and parts of the spleen.

Although mature lymphocytes do not divide, they are very radiosensitive and can be killed directly by radiation. Within 15 minutes of a dose as low as 10 rads, the lymphocyte population can be seen to decrease. In fact, this decrease in the number of lymphocytes can be used to estimate the dose. Recovery of the lymphocyte population is slow.

Granulocytes. This type of leukocyte is produced in the red bone marrow and fights infection by engulfing foreign particles in the body. The granulocytes themselves are radioresistant but their lifespan is short (less than one day). This means that damage to their radiosensitive precursors results in a measurable decrease in the number of granulocytes within a few days of the exposure. Recovery of the granulocyte population is faster than that for lymphocytes.

Platelets. These cytoplasmic fragments are produced in red bone marrow. They are not true cells but nevertheless play an important role in promoting the coagulation of blood. Following acute whole body doses above 50 rads, a decrease in the platelet population will occur in 2 - 5 days. Like granulocytes, they are radioresistant and any decrease in their number is due to damage to their precursor cells, the megakaryocytes. Their longer lifespan, approximately 4 days, means they disappear more slowly than granulocytes.

Erythrocytes. Erythrocytes are responsible for carrying oxygen from the lungs to the various tissues of the body. Comparatively long-lived, they have an average life-span of 4 months. Approximately one week after the exposure, a drop in the number of red blood cells will occur. This decrease is a result of damage to their radiosensitive precursors, the stem cells of the red bone marrow. The latter either stop dividing or die when they attempt to divide. For the victim to have any chance at recovery, some of these stem cells must survive the exposure.

Progress of the Hematopoietic System Syndrome.

Prodromal Stage. Following dose of 200 - 1,000 rads the prodromal stage with its associated NVD will occur within 1 to 5 days of the exposure.

Latent Phase. This asymptomatic period will last 1 to 3 weeks after the prodromal stage.

Illness. Following the latent phase a period of extreme illness begins. Characteristic symptoms of this period include NVD, fatigue, anemia (brought about by the decrease in the red blood cell population), fever, epilation, anorexia and petechial (pinpoint) hemorrhaging on the skin caused by damage to the lining of capillaries.

Death. Death, if it occurs, will be within 2 to 6 weeks of the exposure. The most probable causes of death will be *hemorrhaging* and *infection*. The hemorrhaging is caused by damage to the radiosensitive cells lining the fine blood vessels and is compounded by the reduced population of platelets. Infection occurs because the intestinal bacteria penetrate the damaged lining of the gastrointestinal tract. At the same time, the body's ability to fight infection is reduced due to a decrease in the number of white blood cells.

GASTROINTESTINAL TRACT SYNDROME

The gastrointestinal tract (GI) syndrome is produced by acute whole body exposures from 1,000 to 5,000 rads. Survival is impossible. Death occurs from both the damage to the lining of the GI tract (resulting in *circulatory collapse*) and damage to the hematopoietic system.

Description of Gastrointestinal Tract Lining. Much of the lining of the gastrointestinal tract is covered with small finger-like projections called villi. Villi add to the effective surface area of the lining and thereby increase the capacity of the body to absorb nutrients. The cells on the surface of the villi are constantly migrating towards the tip of the projections where they are sloughed off. Mitotically active cells (crypt cells) at the base of the villi replace those that are lost. The turnover rate of these epithelial cells is high - they have an average life span from 1 to 3 days.

Effect of Radiation on GI Tract Lining. Sufficiently large acute exposures lead to the reproductive death of the rapidly dividing crypt cells. The cells covering the villi continue to be sloughed off but are no longer replaced. This deterioration of the lining of the GI tract then leads to a loss of body fluid, inadequate absorption of nutrients and infection from the intestinal area. Above 1,000 - 1,200 rads the crypt cells are completely destroyed thus preventing any chance for recovery.

Progress of the GI Tract Syndrome.

Prodromal Stage. Within a couple of hours of the exposure, the individual will demonstrate a sharp loss of appetite, upset stomach and apathy. Several hours later NVD will occur.

Latent Phase. By the third day after the exposure, the previous symptoms will have disappeared and the victim will appear healthy. The asymptomatic latent phase will last from 1 to 7 days.

Illness. A period of severe illness will follow the latent phase. This will include NVD, fever, apathy, anorexia and loss of weight.

Death. Death occurs within 3 to 12 days of the exposure. Once the cell renewal mechanism of the GI tract has been completely destroyed and cannot be replaced, death is inevitable. The causes of death include fluid and electrolyte losses (*circulatory collapse*) brought about by the destruction of the lining of the GI tract. These fluid losses also account for the loss of weight, diarrhea and thickening of the blood associated with the GI syndrome. Another contributing cause of death is infection. The latter can occur within 24 hours of the exposure as the bacteria that inhabit the GI tract invade the body across the damaged lining. Damage to the hematopoietic system simultaneously reduces the body's ability to cope with the infection.

CENTRAL NERVOUS SYSTEM (CNS) SYNDROME

The CNS syndrome is produced by acute whole body exposures above 5,000 rads; exposure of the head alone may have similar effects. Survival is impossible. Death results from *respiratory failure* and/or *brain edema* caused from direct or indirect effects on the CNS.

Although the CNS syndrome is not well understood, it most likely involves a combination of cellular and vascular damage. In other words, there may be direct damage to the brain cells by the radiation and indirect damage mediated by effects on the blood vessels of the brain. The latter are known to be damaged by such doses of radiation. Fluid from the blood is lost through the damaged vessel walls into the skull cavity so the pressure inside the skull builds up. Perhaps pressure on certain areas of the brain, i.e., the respiratory center, may be most important, or it may be the change in the blood supply to the brain.

At these high doses, the individual stages of the central nervous system syndrome become so short that they cannot be distinguished. Following such exposures the individual may function coherently for a short while or immediately go into shock. Within hours the symptoms become very severe. Symptoms include vomiting, diarrhea, apathy,

disorientation, and tremors. The victim is also likely to fall into a coma. Death will be due to respiratory failure and/or brain edema and occurs within 30 hours.

1.08.11 Identify risks of radiation exposure to the developing embryo and fetus.

EMBRYOLOGICAL EFFECTS

The Law of Bergonie and Tribondeau indicates that the radiosensitivity of tissue is directly proportional to its reproductive capacity and inversely proportional to the degree of differentiation. It follows that children could be expected to be more radiosensitive than adults, fetuses more radiosensitive than children, and embryos even more radiosensitive.

Both experimental and clinical findings have shown that the human embryo is subject to severe radiation injury. A few of the types of human abnormalities reported in the literature are blindness, cataracts, mental deficiency, coordination defects, deformed arms and legs, and general mental and physical subnormality.

The degree and kind of radiation damage is dependent on the stage of development of the embryo. Most of the major organs in humans are developed during the period from the second to the sixth week post conception. The majority of the gross abnormalities which are produced by irradiation of the embryo occur during this critical period.

Experimentally, doses as low as 25 rad have been shown to be effective in producing development changes if applied during this time. Irradiation of the embryo after the period of major organ development produces delayed and less obvious undesirable effects, such as changes in mental abilities, sterility, etc. A dose of 400 to 600 rad during the first trimester (excluding the first week) of pregnancy is sufficient to cause fetal death and abortion.

1.08.12 Distinguish between the terms "somatic" and "heritable" (or "genetic") as they apply to biological effects.

HERITABLE (GENETIC) EFFECTS

Human body cells normally contain 46 chromosomes, made up of two similar (but not identical) sets of 23 chromosomes each. The 46 chromosomes of the human are believed to contain on the order of 10^4 genes, and it is these genes that, when passed on to the next generation, will determine the physical and psychological characteristics of the individual.

Genes occur in pairs with each pair determining a body characteristic. For most gene pairs, one gene will dominate in producing a given characteristic. Dominant genes are those which produce their effects even when only one of them is present in an individual, while recessive genes produce their effects only when an individual has two of them which are identical. Consequently a recessive gene may be latent for a number of generations, until the union of sperm and egg cells which both contain the same recessive gene.

At conception, the set of hereditary characters from the father are united with those from the mother. As the individual develops, the 23 chromosome pairs (half from each parent) formed by the union of the egg and sperm are almost always duplicated without change. In some instances, however, the chromosome will fail to duplicate itself in every respect, a change occurring in one or more of the genes. This change, called a mutation, is essentially permanent, for the mutant gene is reproduced in its altered form. If this mutation occurs in a body (somatic) cell, there may be some effect on the individual, but the change is not passed to the progeny. However, if the mutation occurs in a germ cell (sperm or ovum) or in the tissues of the organ in which the germ cells are produced, no visible injury will be sustained by the individual, but the effect may appear in future generations.

If a mutation is produced in the germinal tissue of the reproductive organs, the damage is not confined to the immature germ cells then being formed, but all subsequent sperms or ova produced by the affected cell will carry the mutation. A mutation produced in a mature cell (sperm or ovum) is not so harmful, since this mutation will persist only if the actual cells involved give rise to a fertilized egg.

Somatic mutations refer to the injury of the genetic material of the body cells exclusive of the reproductive cells, though somatic mutations are not considered as hazardous as germinal mutations, nevertheless they should not be overlooked. The production of leukemia and of various cancers are effects which have been attributed to mutation in

somatic cells.

It was shown in 1927 that ionizing radiation could produce mutation in the genetic material. Mutations induced by radiation do not differ qualitatively from those which occur naturally, and in any particular instance, it is impossible to determine whether the change occurred naturally or whether it was the result of exposure to radiation. Thus, the net effect of irradiation of the genetic material is to increase the frequency with which mutations occur.

Most of the mutations produced by ionizing radiation are recessive, so that the possibility of a change occurring in the first generation following exposure is slight. However, genetic damage is irreparable, and since a gene determines its own reproduction, the mutant gene will be reproduced and carried by the offspring. Mutated genes persist from generation to generation and accumulate in number until they are either eliminated by natural selection or are mated with identical genes and become expressed as changes in the inherited characteristics of individuals.

Approximately 99% of all mutations are considered to be undesirable. Genetic damage in humans can result in a decrease in life expectancy, inability to produce offspring, an increased susceptibility to disease, or any number of changes of lesser or greater importance.

Mutations of reproductive cells which produced only subtle changes are usually of more importance to a population than mutations which produce gross abnormalities. The more obvious changes usually lead to early death of the individual and reduce fertility in those that survive. Thus the harmful mutant is eliminated from the population by "natural selection." On the other hand, mutant genes which produce less damage may persist much longer, and thereby do harm, although of a less severe character, to a larger number of individuals. Mutations in somatic cells do not present a hazard to the population as a whole, but only affect the individual exposed.

Mutations of genetic material occur normally as a result of background radiation and ordinary physiological processes within the germ cells (called spontaneous mutations). It is generally believed that even the smallest amount of radiation will cause some increase in the normal mutation frequency, or, in other words, there is no threshold for genetic mutations resulting from exposure to ionizing radiations. However, most geneticists agree that the spontaneous mutation rate may be doubled without seriously endangering future generations. The dose of radiation which will double the natural mutation rate in man (doubling dose) is estimated to be greater than 100 rem (1 Sv) per generation. Since the number of children conceived by an individual generally diminishes after the age of thirty, and since the number of persons occupationally exposed is only a small percentage of the total population, the current regulations are believed to be genetically safe.

REFERENCES

1. "Radiation Biology"; Casarett, Alison; Prentice-Hall, Inc.; 1968
2. "A Catalog of Risks"; Cohen, Bernard; Health Physics, Volume 36, pg. 707-722; 1979
3. "Basic Radiation Protection Technology"; Gollnick, Daniel; Pacific Radiation Press; 1983
4. "The Effects on Population of Exposure to Low Levels of Ionizing Radiation"; National Academy of Sciences; 1972
5. "Ionizing Radiation Levels and Effects"; United Nations, Volume II - Effects; New York; 1972
6. "Health Effects of Exposure to Low Levels of Ionizing Radiation"; Biological Effects of Ionizing Radiation (BEIR) Report V; National Research Council; 1990